DATE: February 2015

TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Perioperative Management of Anterior Mediastinal Masses
Evidence Summary

Inclusion Criteria

- Patients with an anterior mediastinal mass scheduled for surgery

Background

Anterior mediastinal masses in children are a heterogeneous group of tumors of the lung, mediastinum, and pleura. Tumors may be primary or metastatic with the most common being lymphoma followed by thymomas, thyroid masses, teratomas, and vascular malformations. Since anterior mediastinal masses differ greatly in type, clinical evolution, size, and topographic distribution, children with an anterior mediastinal mass may present with a spectrum of cardiorespiratory symptoms, including but not limited to dyspnea at rest or exertion, orthopnea, stridor, cough, chest pain, syncope, and upper body edema.

Respiratory decompensation is caused by mechanical compression of the trachea or main bronchi and is exacerbated by awake postural changes or induction of general anesthesia. These cause a critical increase in airway pressure that significantly impairs ventilation and oxygenation. Supine positioning causes a reduction in the transverse diameter of the thorax and cephalad displacement of the diaphragm, increasing the external compression of the mass on the trachea or main bronchi. Central blood volume also increases, increasing the size of a potentially well-vascularized mass. Induction of general anesthesia potentially aggravates a fragile respiratory situation. With general anesthesia the transverse diameter of the thorax is further reduced, the inspiratory tone of the large airways decrease, and the reduction in abdominal muscle tone causes cephalad displacement of abdominal contents. Simultaneous tracheal and bronchial smooth muscle relaxation further exacerbates compression of the large airways following induction of general anesthesia.

Hemodynamic compromise occurs if the heart or great vessels (pulmonary artery and superior vena cava) are surrounded or infiltrated by the mass. The pulmonary arteries are a short distance from the aorta and tracheobronchial tree, protecting them from significant mechanical compression. However, if pulmonary artery diameters are reduced, impaired pulmonary perfusion, hypoxemia, acute right ventricular failure, and cardiac arrest may occur. In contrast to the pulmonary arteries, the superior vena cava is susceptible to mechanical compression with its low intravascular pressure, thin vascular wall, and adjacent firm structures. Reduced venous drainage from the upper half of the body decreases right ventricular filling and cardiac output. Direct compression of the heart is rare, but large tumors, such as lymphomas and thymomas, can cause arrhythmias or low cardiac output from pericardial tamponade and tumor-related pericardial effusion.

Besides chest radiographs, spiral computed tomography (CT) has become an established practice, with modern CT scanners taking less than 30s and allowing the upper body to be elevated without affecting scan quality. CT not only details the size and location of the mass but also permits airway diameter measurements.

The absence of significant symptoms does not correlate with the degree of airway or great vessel compromise whereas the absence of airway or great vessel compromise may not correlate with the severity of symptoms, making the anesthetic management of anterior mediastinal masses challenging. The administration of general anesthesia is associated with increased perioperative morbidity and mortality from acute intraoperative or postoperative cardiorespiratory compromise. Diagnostic biopsy of extramediastinal sites under local anesthesia and mild sedation has been advocated in numerous reports, but many children still require deep sedation or general anesthesia. Pretreatment with radiotherapy or chemotherapy has also been advocated, but this may compromise accurate histopathological diagnosis. Appropriate anesthetic management includes preoperative assessment of the clinical and radiologic findings, discerning airway and great vessel involvement and then risk stratifying the child. Inappropriate preoperative preparation or an inadequate anesthetic technique may result in significant perioperative morbidity or mortality.

Although there are many case reports of perioperative morbidity and mortality for children with anterior mediastinal masses, there are only a few retrospective observational studies attempting to risk stratify patients based upon tumor burden and symptoms. There is no standardized diagnostic algorithm accepted for children with this diagnosis since these algorithms depend on the ability to risk stratify patients; however, multidisciplinary planning from pediatric anesthesiology, pediatric surgery, pediatric cardiovascular surgery, hematology/oncology, critical care, and radiology is necessary to manage these patients perioperatively.

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Critically Analyze the Evidence

The **GRADE criteria** were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of evidence is rated and how a strong versus a weak recommendation is established.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

PICO Question 1: In children with an anterior mediastinal mass, what are the clinical and/or diagnostic factors that increase the risk for anesthetic complications?

Recommendation(s): Strong recommendation with low quality evidence that patients with an anterior mediastinal mass and at least one of the clinical criteria below have an increased risk of perioperative anesthetic complications.

- Three or more symptoms of respiratory distress
- Upper body edema
- Inability to lie flat
- Orthopnea
- Tracheal involvement with cross-sectional area >50%
- Mediastinal mass ratio >0.45%
- Great artery involvement
- Evidence of pericardial tamponade or ventricular dysfunction
- Evidence of pneumonia

Anghelescu et al. published a retrospective cohort study over a 15 year period of 117 patients, who presented with any type of mediastinal mass requiring an anesthetic, to determine specific preoperative clinical and diagnostic imaging features with associated perioperative anesthetic complications. Of the 11/117 patients who experienced an anesthesia-related complication, 77.3% had anterior mediastinal mass. No perioperative deaths occurred in this study and complications described ranged from hypoxia, coughing, wheezing, unplanned intubation with difficult intubation, unplanned intubation, and airway obstruction. Orthopnea, great vessel compression, main-stem bronchus compression, and upper body edema were associated with increased anesthetic-related complications. The presence of a pleural effusion and tracheal compression demonstrated a trend toward anesthesia-related complications. The researchers found no association with mediastinum to mass ratio for anesthesia-related complications. Furthermore, an increased risk of anesthesia-related complications was found with a primary diagnosis of T-cell acute lymphoblastic leukemia. Based on their findings the authors of this study recommend: 1) preoperative multidisciplinary planning and consultation; 2) choosing the least invasive method available to obtain a diagnostic sample, allowing for minimal anesthetic sedation; 3) maintaining spontaneous ventilation to avoid the risk of airway collapse in conjunction with positive pressure ventilation and muscle relaxation; and 4) immediate availability of personnel and equipment for emergency airway management including rigid bronchoscopy and tracheostomy and consideration of some type of cardiopulmonary bypass. [(1)]

Hack et al. reviewed 56 anesthetic records over a 7 year period to identify cases with a high risk of anesthesia-related complications. Complications, which were graded as mild, moderate, or severe, were noted in 11/55 patients (19.6%). No perioperative deaths were observed in this retrospective study. Only one mild cardiac complication of hypotension was noted with a good response to fluid administration. The other ten complications were respiratory, eight of which were mild or moderate, and easily treated with limited intervention. The remaining three severe respiratory complications did not require progression to ECMO or rigid bronchoscopy, but resulted in desaturation severe enough to require intubation or abandonment of the procedure. The presence of the following preoperative clinical signs was associated with an increased risk of anesthesia-related complications: cough p=0.053, dyspnea p=0.053, orthopnea p=0.147, stridor p=0.006, wheezing p=0.096 and SVC obstruction p=0.009. In those patients where a CT scan was available for analysis, respiratory complications occurred almost exclusively in six patients (7 general anesthetics) with tracheal cross sectional area (%CSA) ≤70%. If patients with significant carinal or bronchial compression are excluded, anesthetic respiratory complications were confined to three patients (four general anesthetics) with a %CSA ≤30%. Preoperative administration of steroids, which is often controversial in this patient population, was given to 33% of patients (n=18) at the discretion of the attending hematologist. All 18 patients demonstrated clear evidence of severe airway compromise and/or tumor encasing the great vessels. The presence of the following preoperative clinical signs was associated with an increased risk of anesthesia-related complications in

children who received preoperative steroids: cough p=0.37, dyspnea p=0.002, orthopnea p=0.001, stridor p=0.002, wheeze p=0.009 and SVC obstruction p=0.009. The group treated with steroids was also noted to have a statistically significant smaller tracheal cross sectional area at presentation. Despite the use of preoperative steroids, a clear cancer diagnosis was made in 17/18 (95%) of the subgroup. [(2)]

King et al. reviewed the radiographical correlation between the degree of tracheal compression and size of the mediastinal mass with pulmonary function tests. The mediastinal mass ratio was computed from CT scans in 51 patients. Perioperative data included pulmonary function tests, diagnosis, respiratory symptoms, anesthetic type, and anesthesia-related complications. The patients were divided into groups and analyzed based on the cancer diagnosis and appearance of respiratory symptoms. There was a statistically significant relationship between those patients presenting with non-Hodgkin's lymphoma and the presence of dyspnea at rest and stridor at presentation. Patients with measured mediastinal mass ratio >45% were more likely to have tracheal compression and symptoms of compromised respiratory function. If the subjects presented with any type of respiratory symptom at presentation, both obstructive and restrictive type patterns were observed on pulmonary function tests. Both children with non-Hodgkin's lymphoma and those found to have large tumor burdens (mediastinal mass ratio >45%) were observed to have statistically significant decreased parameters on pulmonary function tests. Thirty of the 51 children (67%) underwent general anesthesia and 15 underwent biopsy with local anesthesia that was supplemented with intravenous sedation (11/15). Only one patient in this series died during the perioperative period. Intraoperative complications were reported in five patients (11%) ranging from converting to general anesthesia, intubation, and repositioning of the airway. All five of these children fully recovered to their baseline preoperative respiratory status. All children who experienced intraoperative complications in this series had non-Hodgkin's lymphoma, a large mediastinal tumor (mediastinal mass ratio median 56%), and symptoms of orthopnea and stridor. [(3)]

Ng et al. retrospectively identified specific anesthetic risk factors in 63 children diagnosed with a mediastinal mass. Forty-eight of the 63 patients received a general anesthetic, with 23 of these patients having an anterior mediastinum mass. A complication rate of 15% in 7 patients was noted with 2 perioperative deaths, secondary to cardiac arrest and severe respiratory obstruction, one of whom was diagnosed with an anterior mediastinal mass. Six of the 7 children with reported complications were diagnosed with an anterior mediastinal mass, as compared to the other 41 patients who also received a general anesthetic. Respiratory symptoms, which were defined as cough, shortness of breath, orthopnea, pleural effusion, use of accessory muscles for breathing, stridor and respiratory arrest were present in 31% of the patients. All 7 of those patients with reported complications had 3 or more of the reported respiratory symptoms upon examination. Only 17% of patients, who had 3 or more respiratory symptoms, had no reported complications. The impact of airway compression on general anesthesia was additionally observed between tracheal compression and an increased risk of anesthesia-related complications. Evidence of tracheal and/or bronchial compression was identified on chest x-ray and/or CT scan in 14 of the 48 patients (29%). Seven of the 41 uncomplicated cases had bronchial but no tracheal compression (p=0.01, sensitivity 85.7%, specificity 100%), suggesting an increased risk when tracheal compression was present. When there was evidence of vascular compromise due to compression of the SVC, IVC, pulmonary artery, or pericardial effusion a trend toward increased anesthetic risk was observed as well. Evidence of vascular compression was found in 13/48 patients (27%). Seven of the 41 uncomplicated cases showed signs of vascular compression by the mediastinal mass. The authors concluded that the effects of tracheal compression, 3 or more respiratory symptoms, and vascular compression increased anesthesia-related complications. [(4)]

Perger et al. retrospectively reviewed their institutional experience in children with anterior mediastinal masses, and further proposed a perioperative management algorithm of these patients. They performed a database search for children diagnosed with lymphoblastic lymphoma, Hodgkin's disease, and large cell lymphoma, who were diagnosed with an anterior mediastinal mass and a critical airway. A critical airway was defined as a tracheal cross sectional area less than 50% predicted, peak expiratory flow rate in the supine position less than 50% predicted, severe narrowing or complete occlusion of one or both of the main stem bronchi; or clinical findings of acute respiratory distress or impending respiratory failure. Forty children were identified, two of whom received pre-operative steroids due to impending respiratory failure. Respiratory symptoms in both patients resolved after the administration of steroids, but a diagnosis was only possible in one of the patients, which was lymphoblastic lymphoma. A diagnosis of lymphoblastic lymphoma was established most commonly by thoracentesis (44%) and bone marrow aspirate (40%), Hodgkin's disease by lymph node biopsy (77%), and in the only case of large cell lymphoma was diagnosed by mediastinal mass biopsy. There were no perioperative deaths reported. Perioperative complications occurred in 4 of the 40 patients (10%). The events were described as apnea, with or without CPR; repositioning with raising the head of the bed resolved symptoms in two of those patients. One patient was transferred to the institution after an acute respiratory arrest at an outside institution. Lastly, one patient with severe respiratory symptoms status post steroids required intubation and initiation of high frequency oscillatory ventilation. [(5)]

Striker et al. reviewed the anesthetic management of children and perioperative course of children with anterior mediastinal mass. Lymphoma was the final diagnosis in 28 of the 45 cases. Thirty-four of the 45 cases (76%) had perioperative signs and symptoms of cardiopulmonary compromise. Twenty-six of the 34 cases (76%) had radiologic evidence of respiratory or cardiovascular decompression. Three of the 45 cases had complications with 2 of the 3 complications related to the administration of anesthesia. Eight of the 26 cases had preoperative signs and radiologic evidence of compressive mass effect and received a muscle relaxant and positive pressure ventilation with one complication in this group. Three cases had radiologic evidence of greater than 50% tracheal compression with all three children having preoperative signs of cardiorespiratory compromise. Each of these children received intravenous sedation with spontaneous ventilation and a natural airway. No anesthetic complications were noted in these children. This study did not comment on the depth of anesthesia as it was not recorded in the electronic medical record, with the general practice at the author's institution to maintain minimal or moderate sedation in children with significant airway obstruction. No child required the use of a rigid bronchoscope to bypass airway obstruction. Due to the small sample size and the low number of complications, a cause-and-effect relationship between the anesthetic technique and perioperative respiratory complications could not be shown. [(6)]

Critical Points of Evidence*

Evidence Supports

- Patients with an anterior mediastinal mass and at least one of the clinical criteria below have an increased risk of perioperative anesthetic complications. – Strong recommendation, low quality evidence
  - Three or more symptoms of respiratory distress
  - Upper body edema
  - Inability to lie flat
  - Orthopnea
  - Tracheal involvement with cross-sectional area <50%
  - Mediastinal mass ratio >0.45%
  - Great artery involvement
  - Evidence of pericardial tamponade or ventricular dysfunction
  - Evidence of pneumonia

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

TCH Evidence-Based Outcomes Center
Anterior Mediastinal Mass and Perioperative Care

Patient with an anterior mediastinal mass scheduled for surgery

Perform clinical assessment
- Respiratory Assessment
  - Orthopnea, Stridor, Wheezing, Cough, Dyspnea, Pleural Effusion, Accessory Muscle Use, Syncope
- Asses for Upper Body Edema

Refer to Preop Imaging
- CXR: determine Mediastinal mass ratio
- CT: determine degree of airway and/or great vessel compromise/compression.
- Echocardiogram: if pericardial effusion identified, bedside TTE to assess for tamponade and function

High Risk^
- ***Three or more symptoms*** of respiratory distress listed in the clinical assessment
- Upper body edema
- Inability to lie flat
- Orthopnea
- Tracheal involvement with cross-sectional area <50%
- Mediastinal Mass Ratio >0.45%
- Great artery involvement
- Evidence of pericardial tamponade or ventricular dysfunction
- Evidence of pneumonia

High risk patient^

No → Proceed with general anesthesia

Yes

Discuss with Oncology

If patient highly symptomatic and must proceed to OR:
- Can preoperative steroids, chemotherapy, or radiation be reasonably administered?

Evidence of pericardial tamponade or ventricular dysfunction with EF <35%

No →
Contact Consultants:
- General Pediatric Anesthesia
- Pediatric Surgery
- ENT: Present in OR with rigid bronch
- Interventional Radiology: PICC line versus central line

Yes

Contact Consultants:
- CV Anesthesia vs. General CV Anesthesia for procedure location.
- CV Surgery for Pericardial Window if effusion present vs. Interventional Cardiology for Pericardial Drain
- CV Perfusion for Bypass/ECMO Standby
- ENT: Present in OR with rigid bronch

Bedside Checklist/ Preoperative Clinical Care
- Time out at bedside with Consultants: Oncology, Pediatric Surgery, Anesthesiology, Intensive Care, Cardiovascular Surgery, ENT, Radiology (Interventional and/or Radiation Oncology), Circulating RN.
- Determine if procedure is high urgency.
- VATS to place LE PIV.
- Type and Cross 2 units PRBC (Irradiated and Leukocyte Reduced) and 1 FFP on call to OR.
- Discuss location of biopsy site: peripheral versus central (established order of biopsy preference: peripheral smear and flow cytometry>bone marrow aspiration>pleural effusion>palpable lymph node>mediastinal mass biopsy)
- Discuss PICC line versus central line
- If feasible, schedule case during “Normal Business Hours.”
- Equipment Ready and Available: 1) Rigid Bronch 2) need for ECMO/ECMO specialists.
- Heme recommendations re: 1) Chemo 2) Radiation 3) Steroids

Anesthetic Management Goals
- Have additional personnel present
- Maintain spontaneous ventilation
- Maintain patient's position of comfort when recumbent
  - May consider lateral or prone position for cardiorespiratory decompensation
- Avoid positive pressure ventilation and muscle relaxants if possible.
- Biopsy under local anesthesia
- If impending respiratory collapse
  - Intubate past obstruction
  - Stent airway with rigid bronchoscope
- Initiate ECMO if impending cardiovascular collapse
- If high risk, has a pericardial effusion or EF <35%: Contact ENT to be present in OR with rigid bronch equipment.
- Consider fluid bolus immediately pre-procedure if tamponade present.

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References

1. Anghelescu, D., Burgoyne, L., Liu, T., Li, C., Pui, C., et al. (2007). Clinical and diagnostic imaging findings predict anesthetic complications in children presenting with malignant mediastinal masses. *Pediatric Anesthesia, 17*, 1090-1098.
2. Hack, H. A, Wright, B., & Wynn R. F. (2008). The anesthetic management of children with anterior mediastinal masses. *Anaesthesia, 63*, 837-846.
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4. Ng, A., Bennett, J., Davies, P., & Morland, B. (2007). Anaesthetic outcome and predictive risk factors in children with mediastinal mass tumors. *Pediatric Blood Cancer, 48*, 160-164.
5. Perger, L., Lee, E. Y., & Shamberger, R. C. (2008). Management of children and adolescents with critical airway due to compression by an anterior mediastinal mass. *Journal of Pediatric Surgery, 43*, 1990-1997.
6. Stricker, P. A, Gurnaney, H. G., & Litman, R. S. (2010). Anesthetic management of children with an anterior mediastinal mass. *Journal of Clinical Anesthesia, 22*, 159-163.

Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

Perioperative Management of Anterior Mediastinal Masses Content Expert Team
Rahul Baijal, MD, Anesthesiology
Lisa Caplan, MD, Anesthesiology

EBOC Team
Andrea Jackson, MBA, RN, Research Specialist
Charles Macias, MD, MPH, Medical Director

Additional EBOC Support
Tom Burke, Research Assistant
Sherin Titus, Research Assistant

No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
   - N/A
3. Literature Review of Relevant Evidence
   - Searched: Pubmed, Cochrane Library, EMBASE
4. Critically Analyze the Evidence
   - 6 nonrandomized studies
5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a Perioperative Management of Anterior Mediastinal Masses evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline. This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.
"Evidence Supports" provides evidence to support an intervention
"Evidence Against" provides evidence against an intervention.
"Evidence Lacking/Inconclusive" indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence*.
The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the perioperative management of anterior mediastinal masses in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

Version History

Date	Action	Comments
Feb 2015	Originally completed	

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